

### **REMARKS**

In the Office Action dated April 18, 2007, the Examiner: (1) objected to the status identifier of claim 1; (2) rejected claims 43 – 60 under 35 U.S.C. § 112; and (3) rejected claims 1 and 38 – 60 under 35 U.S.C. § 101. Applicants respond as follows:

#### **Amendments**

Applicants have amended claim 1 to recite a synthesis step. Support for this step may, for example, be found in paragraph [0266]. Applicants have also made other minor amendments to claim 1 to render it internally consistent.

Applicants have amended claim 43 (and the claims that depend on it) to recite criteria in terms of the presence or absence of bases on the antisense sequence. Because of well known Watson-Crick base pairing rules, and the way that the positions on the antisense and sense sequences are defined, these amendments are supported by the previous pending claim set and throughout the application as filed. See *e.g.*, paragraphs [0147] – [0148] (discussing choice of reference to sense vs. antisense strand for recited factors is merely of convenience). For example, the former criterion of the presence of A at position 19 on the sense sequence has been replaced with the new criteria of the presence of U at position 1 of the antisense sequence. Applicants also have made other minor amendments to claim 43 to render it internally consistent.

Furthermore Applicants have amended claims 42 and 44 – 60 to provide antecedent basis for each of the limitations and/or to render them internally consistent.

#### **New Claims**

Applicants have added new claims 61 – 85.

New claim 61 is directed to a method of selecting a siRNA sequence. The method contains steps (a) – (d) that are similar to steps (a) – (d) of currently pending claim 1. Step (e) comprises generating an output. Support for this new claims may be found in previously pending claim 1 and within Example V, pars. [0302] – [0306], reflecting the generation of a list of the top 10 siRNA for Bcl-2 that were generated by

Formula VIII, and within Example VI and Table V, par. [0307], providing values generated by Formulas VIII and IX as applied to a number of targets.

New claims 62 - 66 are similar to currently pending claims 38 – 42. However, instead of depending on claim 1, they depend on claim 61.

New claim 67 depends on claim 61 and specifies that the output is in a form that is readable by a computer. Support for this amendment may, for example, be found in paragraphs [0166] and [0217].

New claim 68 is directed to a method of selecting a siRNA sequence. The method contains steps (a) – (d) that are similar to steps (a) – (d) of currently pending claim 43. Step (e) comprises generating an output. Support for this new claims may be found in previously pending claim 43 and within Example V, pars. [0302] – [0306], reflecting the generation of a list of the top 10 siRNA for Bcl-2 that were generated by Formula VIII, and within Example VI and Table V, par. [0307], providing values generated by Formulas VIII and IX as applied to a number of targets.

New claim 69 depends on claim 68 and specifies that the output is in a form that is readable by a computer. Support for this amendment may, for example, be found in paragraphs [0166] and [0217].

New claims 70 - 77 are similar to currently pending claims 44 – 51. However, instead of depending on claim 43, they depend on claim 68.

New claims 78 –81 specify that the complementarity between the candidate and target sequence is 100%. Support for these claims may for example, be found in paragraphs [0260] – [0266].

New claims 82 and 84 specify that the synthesizing is by chemical synthesis. New claims 83 and 85 specify that the synthesizing is by enzymatic synthesis. Support for these claims may for example, be found in paragraph [0263].

### **Response to Objection to Status Identifier**

The Examiner objected to the status identifier “previously introduced.” In the presently pending claim set, Applicants have not used this reference. Accordingly, Applicants request that the objection be withdrawn.

**Response to Rejection Under 35 U.S.C. § 112, ¶ 2**

The Examiner rejects claims 43 – 60 under 35 U.S.C. § 112, ¶ 2.

First, the Examiner rejects claims 55 – 57 and asserts that there is insufficient antecedent basis for the criteria of GC content, the presence of at least 2A or U bases at position 15 – 19 and an internal repeat that is not stable at greater than 50 °C. Applicants have amended each of these claims to clarify that these three criteria are part of group of criteria within a set of criteria that are to be applied to the candidate siRNA sequence is selected. (Applicants have also changed the reference for the 2A or U bases to positions 1 – 5 of the antisense sequence.) Applicants note that although the set of criteria has been increased from that recited in claim 43, so too has then number of criteria that must be applied.

By way of example, claim 43, recites applying at least one of eight criteria. In claim 55 as amended there are eleven criteria in the set (the eight from claim 43 and the three additional criteria noted above). From this set, one must apply at least four of the criteria. Thus, the set of criteria that are to be applied in claim 55 must comprises at least one, and up to four of the criteria recited in claim 43, and claim 55 is a properly worded dependent claim.

Claim 56 as amended is analogous to claim 55, but requires the application of at least five of the recited criteria.

Claim 57 as amended recites the specific criteria from claim 43 to be applied, as well as additional criteria, and that the siRNA sequence is selected if it satisfies each of the criteria. Claim 60 was rejected on similar grounds and has been amended in a similar manner.

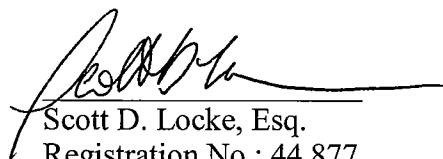
Second, the Examiner objected to claim 43 for reciting a similarity of at least 79% when paragraph [0117] explicitly defines the phrase substantially similar as of at least 90%. As noted above, Applicants have amended claim 43 to remove reference to the degree of similarity between the sense sequence and the target. Instead, the claim references the degree of complementarity between the target and the antisense sequence. As par. [0114] recites, substantial complementarity is defined as complementarity of 79% or greater.

**Response to Rejection Under 35 U.S.C. § 101**

The Examiner asserted that previously pending claims 1 and 38 – 60 were not patentable because they did not involve a step of physical transformation, or produce a useful, concrete or tangible result. Applicants respectfully disagree with basis for the rejection. However, in order to further prosecution, Applicants have amended both of the pending independent claims, claims 1 and 43, by adding a step of synthesizing a siRNA molecule. Applicants have also made other minor amendments to these claims to render them internally consistent. Support for these amendments is identified above. Accordingly, Applicants request that the rejection be withdrawn.

Applicants authorize the Patent Office to charge the Deposit Account No. 11-0171 for the additional claims – one independent claim more than three and twenty-five additional claims. Applicants also authorize the Patent Office to charge the afore-referenced deposit account for any additional fees that are deemed necessary.

Respectfully submitted,

  
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Scott D. Locke, Esq.  
Registration No.: 44,877  
Attorney for Applicants

Kalow & Springut LLP  
Telephone No.: (212) 813-1600